JWMR
Journal of Wound Management and Research
J Wound Manag Res 2021 June;17(2):85-93
https://doi.org/10.22467/jwmr.2020.01277
pISSN 2586-0402
eISSN 2586-0410

Degrees of Arterial Stenosis and Other Factors Related with Diabetic Foot Wound Severity

Song Hyun Han, Dong In Jo, Cheol Keun Kim, Soon Heum Kim

Department of Plastic and Reconstructive Surgery, Konkuk University Chungju Hospital, Konkuk University School of Medicine, Chungju, Korea

Abstract

Background: Few studies have addressed which blood vessels are affected by arterial stenosis in patients with diabetic foot (DF) and the severity thereof. Furthermore, whether the severity of arterial stenosis is significantly correlated to DF severity was yet to be established. We analyzed the association between the severity of arterial stenosis and DF wound severity, along with a variety of relevant factors.
Methods: Seventy-one cases hospitalized with DF were evaluated. To assess the degree of arterial stenosis of the five major arteries of the lower extremity (femoral, popliteal, anterior tibial, posterior tibial and peroneal artery), we performed computed tomography angiography, and quantified arterial stenosis using Bollinger scores. We then assessed DF severity and calculated self-reported wound scores. We also analyzed factors that can affect DF severity and the degree of arterial stenosis in the lower extremities.
Results: There was no significant association between the mean total Bollinger score and wound severity. Albumin, protein, and Bollinger scores of femoral arteries showed significant association with wound severity, and age and ankle-brachial index (ABI) showed significant association with mean total Bollinger scores ($P<0.05$). Albumin and Bollinger scores of femoral arteries had significant association with wound severity, and age and ABI showed significant association with mean total Bollinger scores ($P<0.05$).
Conclusion: There was no significant association between the degree of vascular obstruction and the severity of DF. Our results indicate that surgeons should consider the other factors above to ensure appropriate management of patients with DF and assess the prognosis.

Keywords: Diabetes mellitus; Diabetic foot; Peripheral arterial disease; Arterial occlusive diseases; Computed tomography angiography

Introduction

Peripheral arterial occlusive disease (PAOD) refers to atherosclerosis below the bifurcation of the abdominal aorta [1]. It is a major contributor to diabetic foot (DF) in patients with diabetes mellitus (DM) [2]. The prevalence of PAOD is up to 6 times higher in the elderly with DM than in those without DM [3]. Patients with both DF and PAOD show lower limb ischemia with poor wound healing; as such, they are vulnerable to lower limb amputations [4]. Therefore, to manage foot problems in patients with DF, the risk factors associated with PAOD must be identified [2]. The general risk factors of atherosclerosis, such as systolic hypertension, smoking, dyslipidemia and old age, are closely associated with PAOD progression [5,6]. Moreover, high HbA1c, low-density lipoprotein cholesterol and smoking may also be risk factors for PAOD in patients with DM [7,8].

To date, PAOD has been recognized as an independent disease entity. Its severity is decided based on imaging studies, symptom severity, resting pain and tissue damage, as previously formulated by the Fontaine and Rutherford classification [9]. However, few studies have investigated whether the degree of peripheral arterial stenosis has significant association with the severity of DF in patients with DM.

In the present study, we explored the association between the arterial stenosis se-

Original Article

Received: September 10, 2020
Revised: February 25, 2021
Accepted: March 17, 2021

Corresponding author:
Soon Heum Kim, M.D., Ph.D.

Department of Plastic and Reconstructive Surgery, Konkuk University Chungju Hospital, Konkuk University School of Medicine, 82 Gugwon-daero, Chungju 27376, Korea
Tel: +82-43-840-8860
Fax: +82-43-840-9862
E-mail: plastics7@gmail.com

verity and wound severity. Furthermore, our analysis aimed to identify factors that may affect the degree of arterial stenosis in the lower extremities, as defined using computed tomography angiography (CTA), and DF severity.

Methods

Enrolled patients and setting

We performed a retrospective review of the medical records of 71 cases with DF who were hospitalized at our medical institution between April 2014 and April 2019. The inclusion criteria were as follows: (1) diagnosis of DM; (2) diagnosis of DF; and (3) available CTA of arteries in the lower extremities. The exclusion criteria were as follows: (1) previous history of percutaneous angioplasty; and (2) previous history of drug use that could affect arterial stenosis severity, such as aspirin, clopidogrel, cilostazol and pentoxifylline [10].

We enrolled a total of 71 cases with DF who underwent CTA of the arteries in the lower extremities. We classified the blood vessels of the lower extremity into five major arteries for each DF patient and evaluated arterial stenosis using the Bollinger score, and scored DF wound severity by a self-reported wound score system. The association between the severity of arterial stenosis and DF wound severity was statistically analyzed. In addition, we analyzed statistically whether baseline characteristics were associated to DF wound severity and arterial stenosis. The study was approved by the Institutional Review Board of Konkuk University Chungju Hospital (IRB No. KUCH 2019-12-041). The need for informed consent was waived because the study was retrospective.

CTA of arteries in the lower extremities

To analyze the status of the vessels, the arteries of the lower extremities were classified into five major arteries or segments: femoral artery (FA), popliteal artery (PopA), anterior tibial artery (ATA), posterior tibial artery (PTA), and peroneal artery (PerA).

CTA of the arteries of the lower extremities was performed using a 320-slice CT scanner (Aquilion ONE; Toshiba Medical Systems, Tokyo, Japan), in which the patients were placed in a fixed supine position. Prior to this, they were intravenously injected with iopamidol (Iopamiro 370/150; Bracco Imaging, Seoul, Korea) via the antecubital vein using an 18-gauge intravenous catheter at a rate of 4 mL/sec to ensure that 120 mL was injected within 30 seconds [11].

Table 1. Bollinger scoring matrix

Location	Occlusive pattern			
	Plaque ≤25%	Stenosis ≤50%	Stenosis >50%	Occlusions
Single	1	2	4	-
Multiple ≤50% segment	2	3	5	13
Multiple >50% segment	3	4	6	15

Assessment of arterial stenosis severity using CTA

The scoring system developed by Bollinger et al. [12] was used to assess the angiographic findings. This system consists of an additive score that describes the severity and extent of arterial stenosis in each segment of the artery. The score defines four categories according to the severity of arterial stenosis: (1) complete occlusion of the lumen, (2) stenosis >50% of the luminal diameter, (3) stenosis ≤50% but >25% of the diameter, and (4) plaques impinging on ≤25% of the diameter. Each type of lesion is then further categorized based on its extent: (1) single lesion, (2) multiple lesions affecting ≤50% of the artery 5 segments, and (3) multiple lesions affecting >50% of the segment. Scores are assigned according to the severity of each category (Table 1). For example, an isolated subtotal stenosis is 4 points. If multiple plaques with stenosis of less than 25% of the lumen spread over half of the segment, 3 points are added, so the additive score is 7 (4+3).

There are several rules to prevent inappropriate scoring: (1) in presence of an occlusion lesion, stenosis and plaque are not considered; if there is occlusion affecting less than 50% of the segment, the score number remains 13 even if there is plaque or stenosis in the non-occluded part. (2) When both categories of stenoses are present (>50% and ≤50%), plaques ≤25% are not considered; (3) for each occlusive pattern, only one category of extent is applied. When there are plaques ≤25% that affect more than 50% of a segment, the score number applies only to 3 and not 2 or 1. In the present study, the Bollinger scoring system was applied to two suprapopliteal level arterial segments (the superficial FA and PopA) and three infrapopliteal level ones (ATA, PTA, and PerA). Total scores were calculated as the sum of the scores for the suprapopliteal and infrapopliteal segments.

Assessment of DF wound severity

The criteria for assessing DF severity are as follows: the score is indicated in parentheses.

I. Depth: skin or subcutaneous tissue (1), tendon, muscle, fascia (2), bone or joint (3).

https://doi.org/10.22467/jwmr.2020.01277

II. Size: <1 cm^2 (1), 1–3 cm^2 (2), >3 cm^2 (3).
III. Infection: Inflammation (erythema, local heating) (1), gangrene (mummification, pus) (2).

After analyzing each category, each score is added to give the wound severity score.

Patient evaluation and criteria

The baseline characteristics of the patients included age, sex, body mass index (BMI), wound location, wound depth, wound size, type of infection, duration of DM, smoking status, hypertension, laboratory measurements performed on the day of hospitalization (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], albumin, total protein, and white blood cell [WBC] count), and ankle-brachial index (ABI).

Statistical analysis of patient data

All data were expressed as mean±standard deviation. Statistical analysis was performed using SPSS version 23 (IBM Corp., Armonk, NY, USA). Univariable regression analysis was used to analyze the association between wound severity and mean total Bollinger score. The Bollinger scores of each segment were also examined for association with wound severity, using univariable regression analysis. Multivariable regression analysis was used to additionally analyze whether the Bollinger score of each segment was associated to wound severity. To identify factors affecting wound severity and mean total Bollinger scores, a univariable regression analysis was performed. Multivariable regression analysis was performed on the variables showing significant differences in the univariable regression analysis. All P-values <0.05 were considered statistically significant.

Results

Baseline characteristics of the patients

Our clinical series of cases (n=71) comprised 61 unilateral cases and 5 bilateral cases. From the cases, 35 cases (53.0%) were right, 26 cases (39.4%) were left and 5 cases (7.6%) were both right and left (bilateral). There were 49 men (69.0%) and 22 women (31.0%) with a mean age of 60.9±11.3 years. Out of the patients, 56 cases (78.9%) had arterial stenosis and 15 (21.1%) had no arterial stenosis. The mean wound severity score was 6.1±1.9 and the mean total Bollinger score was 19.5±17.4. The patients' DM had been diagnosed for an average of 16.2±9.9 years. There were 47 cases (66.2%) with a history of smoking and 24 cases (33.8%) were nonsmokers. The 31 cases (43.7%) had hypertension. The mean BMI was 24.3±4.0 kg/m^2 and the mean ABI was 1.0±0.3. The average values of the laboratory measurements performed on the day of hospitalization were as follows: CRP, 9.9±8.8 mg/dL; ESR, 45.3±18.9 mm/hr; albumin, 3.1±0.6 g/dL; total protein, 6.7±0.8 g/dL; WBC count, 12.8± 7.8 ×10^3/μL (Table 2).

Table 2. Baseline and clinical characteristics of the patients

Variable	Value
Age (yr)	60.9±11.3
Sex	
Men	49 (69.0)
Women	22 (31.0)
Laterality	
Right	35 (53.0)
Left	26 (39.4)
Both	5 (7.6)
Arterial stenosis	
Positive	56 (78.9)
Negative	15 (21.1)
Wound score	6.1±1.9
Bollinger score	
Femoral artery	3.9±3.9
Popliteal artery	2.6±3.3
Anterior tibial artery	4.8±5.4
Posterior tibial artery	4.5±5.2
Peroneal artery	3.6±4.3
Mean total Bollinger score	19.5±17.4
DM period (yr)	16.2±9.9
Smoking status	
Smoking	47 (66.2)
Non-smoking	24 (33.8)
Hypertension	31 (43.7)
Body mass index (kg/m^2)	24.3±4.0
Laboratory measurements	
CRP (mg/dL)	9.9±8.8
ESR (mm/hr)	45.3±18.9
Albumin (g/dL)	3.1±0.6
Protein (g/dL)	6.7±0.8
WBC (10^3/μL)	12.8±7.8
ABI	1.0±0.3

Values are presented as mean±SD or number (%).
DM, diabetes mellitus; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell count; ABI, ankle-brachial index.

Table 3. Associations between wound severity and Bollinger scores

Variable	Wound severity			
	Univariable regression analysis		Multivariable regression analysis	
	B (95% confidence interval)	P-value	B (95% confidence interval)	P-value
Bollinger score				
Femoral artery	0.136 (0.030 to 0.242)	0.013[a)]	0.152 (0.003 to 0.300)	0.045[a)]
Popliteal artery	0.061 (–0.071 to 0.193)	0.362	–0.038 (–0.193 to 0.117)	0.626
Anterior tibial artery	0.039 (–0.042 to 0.121)	0.337	–0.033 (–0.146 to 0.079)	0.557
Posterior tibial artery	0.060 (–0.024 to 0.143)	0.159	0.013 (–0.115 to 0.140)	0.843
Peroneal artery	0.075 (–0.026 to 0.176)	0.144	0.030 (–0.113 to 0.174)	0.673
Mean total Bollinger score	0.023 (–0.002 to 0.048)	0.068		

[a)]Statistical significance at $P<0.05$.

Association between the severity of arterial stenosis and DF wound severity

Univariable regression analysis showed that Bollinger score of FA showed significant association with wound severity. However, there was no significant association between wound severity and mean total Bollinger score. In multivariable regression analysis, Bollinger score of FA showed a significant association with wound severity (Table 3). A scatter plot was used to show the relationship between the Bollinger score and wound severity (Fig. 1).

Factors affecting wound severity and Bollinger score

Univariable regression analysis showed that albumin and protein showed significant association with wound severity. In multivariable regression analysis, only albumin had a significant association with wound severity (Table 4). Univariable regression analysis showed that age and ABI had a significant association with mean total Bollinger score. In multivariable regression analysis of mean total Bollinger score, both age and ABI showed significant association (Table 5). Duration of DM, smoking status, BMI, ESR, CRP and WBC count were not associated with wound severity and mean total Bollinger score. Hypertension was not associated with wound severity or mean total Bollinger score.

Pattern of arterial occlusion by segment

The normal ratio of the FA was the lowest among all the arterial segments (29.6%), while the ratio of ≤50% stenosis plus ≤25% plaque was the highest (47.9%). However, the proportion of occlusion plus >50% stenosis was the lowest (22.5%) in the FA. Of the arterial segments, both the ATA and PTA were found to have the highest degree of occlusion (18.3%). The normal ratio of the PopA was the highest (46.5%). With regards to the total value according to occlusive pattern, occlusion and >50% stenosis accounted for 25.3%, stenosis ≤50%, plaque ≤25% and normal accounted for 74.6% (Table 5). Mild obstruction (≤50% of lumen) occupied a large portion (Table 6).

Discussion

Patients with DM show metabolic derangement and alterations in arterial structure and function [13]. Such alterations may occur even prior to the clinical diagnosis of DM [14]. Several hypotheses have been proposed to explain the pathogenesis of DF. According to the hemodynamic hypothesis, the onset of hyperglycemia in the early stages of DM leads to derangements in blood flow, resulting in increases in flow, capillary filtration capacity, and microvascular pressure. This likely results in structural alterations in diabetic microangiopathy, such as a thickened basement membrane with microvascular sclerosis. The resulting decrease in microvascular vessel elasticity disturbs vasodilatation and may be coupled with impaired secretory functions in the endothelium. It may then also lower the hyperemic response in patients with DM [3]. Additionally, sympathetic innervation of the microvasculature is disturbed by autonomic neuropathy and thereby causes a loss of vasoconstriction in patients with DM, which may eventually lead to changes in blood flow through the capillaries and arteriovenous anastomoses [3].

Although severe arterial stenosis has a significant effect on wound healing, major amputation, and mortality in patients with DF [15], few studies have investigated the association between DF wound severity and arterial stenosis severity. In the present study, only the Bollinger score of the FA showed a sig-

https://doi.org/10.22467/jwmr.2020.01277

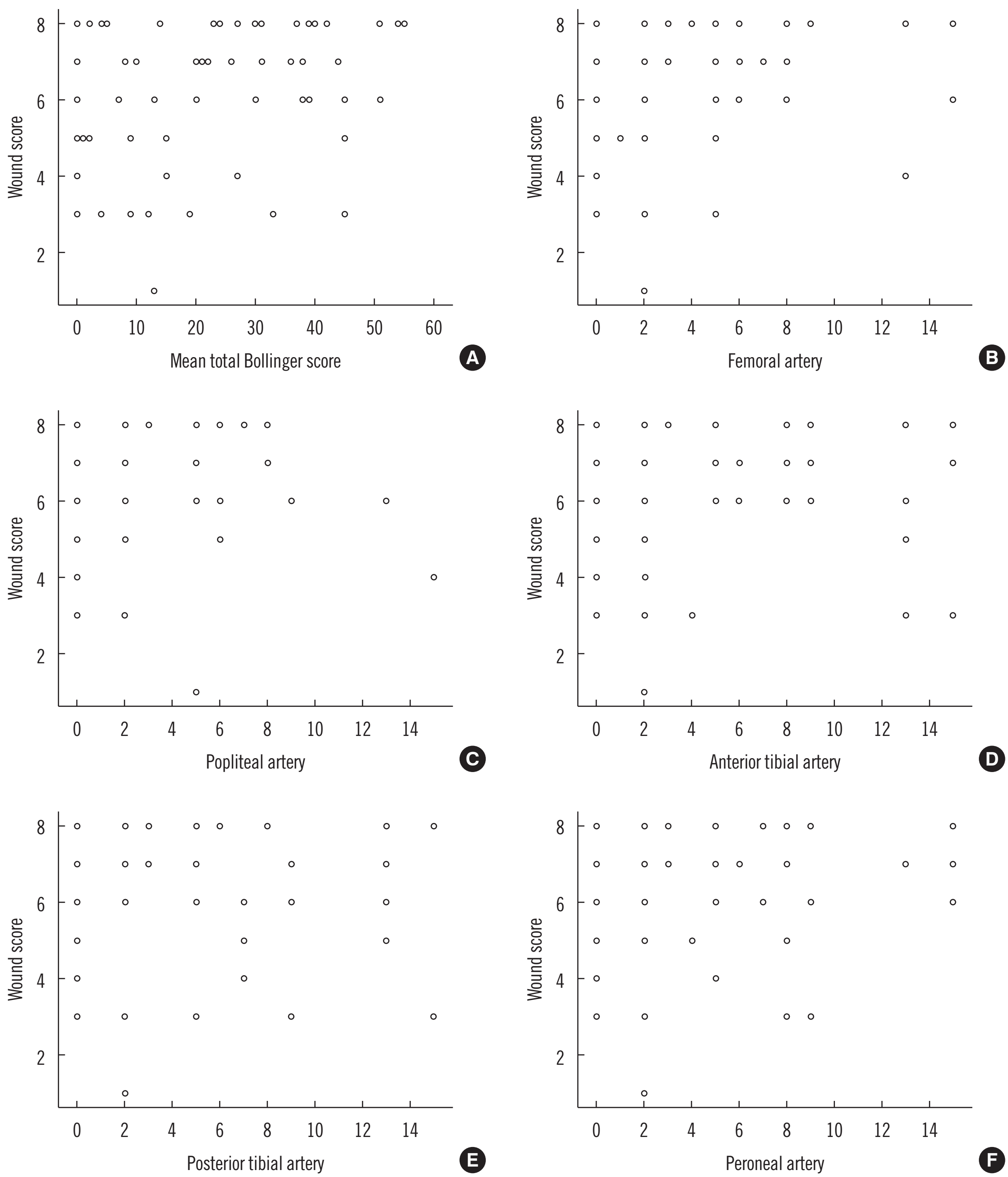

Fig. 1. Scatter plot of Bollinger score and wound severity. (A) Scatter plot of mean total Bollinger score and wound severity. (B) Scatter plot of Bollinger score of femoral artery and wound severity. There was a significant association in regression analysis. (C) Scatter plot of Bollinger score of popliteal artery and wound severity. (D) Scatter plot of Bollinger score of anterior tibial artery and wound severity. (E) Scatter plot of Bollinger score of posterior tibial artery and wound severity. (F) Scatter plot of Bollinger score of peroneal artery and wound severity.

nificant association with wound severity. There was no significant association between mean total Bollinger score and wound severity. Therefore, even though the prevalence of arterial stenosis increases in patients with DM, the severity of arterial stenosis is not associated with DF wound severity. The authors' opinion is that Bollinger scores of more distal arterial segments would have less significant association with wound severity because of more active compensatory mechanisms

JWMR

Table 4. Factors affecting wound severity

Variable	Wound severity			
	Univariable regression analysis		Multivariable regression analysis	
	B (95% confidence interval)	P-value	B (95% confidence interval)	P-value
Sex	–0.458 (–1.399 to 0.483)	0.335		
Smoking status	0.793 (–0.114 to 1.699)	0.086		
Hypertension	–0.457 (–1.334 to 0.419)	0.302		
Age (yr)	–0.022 (–0.061 to 0.016)	0.253		
DM period (yr)	–0.022 (–0.066 to 0.022)	0.316		
Body mass index (kg/m^2)	–0.015 (–0.124 to 0.094)	0.791		
Laboratory measurements				
CRP (mg/dL)	0.039 (–0.011 to 0.088)	0.123		
ESR (mm/hr)	0.011 (–0.015 to 0.037)	0.391		
Albumin (g/dL)	–1.216 (–1.897 to –0.535)	0.001[a)]	–1.162 (–1.989 to –0.334)	0.007[a)]
Protein (g/dL)	–0.552 (–1.076 to –0.290)	0.039[a)]	–0.144 (–0.721 to 0.433)	0.619
WBC (10^3/μL)	0.036 (–0.020 to 0.092)	0.209		
ABI	–1.212 (–2.615 to 0.191)	0.089		

DM, diabetes mellitus; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cells; ABI, ankle-brachial index.
[a)]Statistical significance at $P<0.05$.

Table 5. Factors affecting mean total Bollinger scores

Variable	Mean total Bollinger score			
	Univariable regression analysis		Multivariable regression analysis	
	B (95% confidence interval)	P-value	B (95% confidence interval)	P-value
Sex	–3.526 (–12.443 to 5.391)	0.433		
Smoking status	2.172 (–6.569 to 10.913)	0.622		
Hypertension	6.193 (–2.025 to 14.411)	0.137		
Age (yr)	0.800 (0.486 to 1.114)	0.000[a)]	0.507 (0.113 to 0.902)	0.013[a)]
DM period (yr)	0.182 (–0.235 to 0.599)	0.387		
Body mass index (kg/m^2)	–0.044 (–1.075 to 0.987)	0.933		
Laboratory measurements				
CRP (mg/dL)	–0.365 (–0.831 to 0.101)	0.122		
ESR (mm/hr)	–0.001 (–0.244 to 0.242)	0.994		
Albumin (g/dL)	3.262 (–3.696 to 10.219)	0.353		
Protein (g/dL)	–1.212 (–6.320 to 3.896)	0.637		
WBC (10^3/μL)	–0.217 (–0.751 to 0.317)	0.421		
ABI	–28.165 (–41.313 to –15.016)	0.000[a)]	–20.926 (–34.662 to –7.190)	0.003[a)]

DM, diabetes mellitus; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cells; ABI, ankle-brachial index.
[a)]Statistical significance at $P<0.05$.

such as collateral circulation development. However, the FA is a proximal main vessel with less compensatory mechanisms, which may explain why it particularly can affect DF severity. Of the 71 cases, 15 (21.1%) had no arterial stenosis lesions in their CTA, even though their DF required hospitalization. With regards to the total value according to occlusive pattern, occlusion and >50% stenosis accounted for 25.3%, while stenosis ≤50%, plaque ≤25% plaque, and normal accounted for

 https://doi.org/10.22467/jwmr.2020.01277

Table 6. Distribution of cases according to occlusive pattern

Case	Occlusive pattern				
	Occlusions	Stenosis >50%	Stenosis ≤50%	Plaque ≤25%	Normal
Femoral artery	5 (7.0)	11 (15.5)	18 (25.4)	16 (22.5)	21 (29.6)
Popliteal artery	2 (2.8)	6 (8.5)	17 (23.9)	13 (18.3)	33 (46.5)
Anterior tibial artery	13 (18.3)	13 (18.3)	6 (8.5)	10 (14.1)	29 (40.8)
Posterior tibial artery	13 (18.3)	9 (12.7)	10 (14.1)	10 (14.1)	29 (40.8)
Peroneal artery	5 (7.0)	13 (18.3)	9 (12.7)	16 (22.5)	28 (39.4)
Total	38 (10.7)	52 (14.6)	60 (16.9)	65 (18.3)	140 (39.4)

Values are presented as number (%).

74.6%. The rate of obstruction ≤50% of the vessel lumen was much higher. Therefore, DF wound severity could not be predicted by circulation alone. The aforementioned functional and structural changes of the microvasculature, neuropathy, foot trauma, foot deformity, foot edema, and callus formation seem to be more important factors in DF than arterial stenosis severity.

Many scoring systems have been proposed and used for the evaluation of DF wound and critical limb ischemia. The Wound, Ischemia, and foot Infection (WIfI) score system made by modifying many of these score systems is currently being widely used. The system conducts the assessment using three major factors (wound, ischemia, foot infection) that influence amputation risk and clinical management [16]. Among the factors, ischemia is evaluated using toe pressure or transcutaneous oximetry or ABI. In the present study, we wanted to analyze the relationship between the angiographic finding and the severity of the DF wound itself. Therefore, the WIfI score system, which includes ischemia evaluation, could not be used in our study.

Previous studies have reported that the pattern of atherosclerotic lesions is more severe in distal segments and more diffuse in patients with DM than in those without DM [17]. According to Graziani et al. [18], lesions in the infrapopliteal arteries, especially the ATA and PTA, show more occlusion than those in proximal segments. In the current study, the mean Bollinger score and the proportion of arterial occlusions were higher in the ATA and PTA than in other arterial segments. In the FA proximal segment, the rate of obstruction of >50% of the lumen was 22.5%, which was lower than that in the infrapopliteal segments. In addition, the rate of obstruction ≤50% of the lumen was 47.9% in the FA, which was higher than that in the infrapopliteal segments. It is unknown why arterial stenosis is diffuse and more severe in the distal segment in patients with DM. According to van der Feen et al. [17], DM may interfere with the compensatory enlargement of vessel circumference that preserves vessel lumen diameter even with atherosclerotic plaques. As a result, it may lead to a pattern of diffusely narrowed arteries. Furthermore, remodeling leading to paradoxical shrinkage, with subsequent diffuse narrowing and occlusion of distal vessels, may cause different patterns in the DM. It is estimated that these events are more likely to occur in distal vessels, and our results support this.

The PopA segment had the lowest mean Bollinger score; 46.5% of segments had no atherosclerotic lesion, and the proportion of stenosis >50% was the lowest (11.3%). Among all segments, the PopA showed the lowest arterial stenosis severity. We propose that the chance of atherosclerotic lesions is relatively low in the PopA because it is the shortest segment and the popliteal region is a joint, with a large range of motion, and fast, uncongested blood flow. Additionally, 29.6% of FA segments were normal. This was the lowest proportion among the segments and may have occurred because the FA is the longest of the segments; therefore, the chance of atherosclerotic lesions may be higher.

Many serum inflammatory markers are used to determine whether a wound infection has occurred. Procalcitonin, ESR, and CRP show reasonable accuracy for predicting DF wound severity, and the elevation of these values predicts the occurrence of osteomyelitis and arterial stenosis with good accuracy and acceptable sensitivity [19]. Serum WBC count is also a significant marker for distinguishing infection, although its sensitivity and specificity are lower than those of ESR and CRP [20]. In the present study, WBC count, CRP and ESR did not show any significant association with wound severity and mean total Bollinger score.

In chronic diseases such as DM, poor nutritional status affects prognosis. Serum albumin is widely used as a nutritional indicator [21,22]. Lower serum albumin levels affect non-healing ulcers and prognosis in DF. Serum albumin and protein level were significantly associated with wound severity in the present study. Therefore, while the treatment of the wound itself is important, the overall improvement of the nutritional condition is also likely to be important.

The prevalence of arterial stenosis increases with age [4]. In the present results, there was a positive association between age and mean total Bollinger score, but age had no significant association with wound severity. Therefore, as age increases, arterial stenosis tends to get worse, but this is not associated with increased DF severity. ABI, which is widely used as a simple method for evaluating arterial stenosis, showed negative association with mean total Bollinger score and no significant association with wound severity. The negative association between ABI and mean total Bollinger score verifies that ABI indeed can be used as an indirect index of arterial stenosis.

As per popular perception, smoking status was estimated to affect wound severity and arterial stenosis, but there was no significant association in the present study [15]. Nevertheless, smoking interferes with wound healing via various mechanisms and reduces tissue blood flow and oxygen supply. It also causes microvascular alterations, such as impaired vasodilation, sympathetic stimulation by nicotine, atherosclerosis of the lower extremities and cellular oxygen metabolism disturbances due to carbon monoxide. Chronic hypoxia reduces fibroblast activity and interferes with collagen synthesis and angiogenesis [23]. Cigarette smoking increases the risk of DF-related amputation and smoking has been associated with serious postoperative complications. Smoking cessation for more than three weeks prior to surgery reduced the incidence of impaired wound healing and reduced postoperative morbidity [23].

As shown in the current study, diverse factors, such as albumin, protein, age and ABI, had a significant association with arterial stenosis and DF severity. However, the degree of arterial stenosis was not significantly associated with wound severity, and patients with normal blood vessels were also hospitalized with DF and had to undergo surgery. Therefore, rather than evaluating patients with DF based on the severity of blood vessel obstruction, clinicians should consider a multitude of factors to plan the diagnosis and treatment of DF.

If research methods used in the study could quantitatively measure the degree of vascular obstruction or peripheral blood flow in the arteries, more objective data could have been obtained. Future studies should involve a larger number of cases and focus on a wider variety of factors, as well as on the location of arterial stenosis in blood vessels. Such research may inform more specific treatment for diabetic arteriosclerosis.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

ORCID iDs

Song Hyun Han https://orcid.org/0000-0002-2726-2583
Dong In Jo https://orcid.org/0000-0002-3075-4482
Cheol Keun Kim https://orcid.org/0000-0003-2126-9749
Soon Heum Kim https://orcid.org/0000-0001-9773-4753

References

1. Stoffers HE, Rinkens PE, Kester AD, et al. The prevalence of asymptomatic and unrecognized peripheral arterial occlusive disease. Int J Epidemiol 1996;25:282-90.
2. Kallio M, Forsblom C, Groop PH, et al. Development of new peripheral arterial occlusive disease in patients with type 2 diabetes during a mean follow-up of 11 years. Diabetes Care 2003;26:1241-5.
3. Kabbani M, Rotter R, Busche M, et al. Impact of diabetes and peripheral arterial occlusive disease on the functional microcirculation at the plantar foot. Plast Reconstr Surg Glob Open 2013;1:e48.
4. Thiruvoipati T, Kielhorn CE, Armstrong EJ. Peripheral artery disease in patients with diabetes: epidemiology, mechanisms, and outcomes. World J Diabetes 2015;6:961-9.
5. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. Circ Res 2015;116:1509-26.
6. Berard AM, Bedel A, Le Trequesser R, et al. Novel risk factors for premature peripheral arterial occlusive disease in non-diabetic patients: a case-control study. PLoS One 2013;8:e37882.
7. Forrest KY, Becker DJ, Kuller LH, et al. Are predictors of coronary heart disease and lower-extremity arterial disease in type 1 diabetes the same? A prospective study. Atherosclerosis 2000;148:159-69.
8. Faghihimani E, Darakhshandeh A, Feizi A, et al. Evaluation of peripheral arterial disease in prediabetes. Int J Prev Med 2014;5:1099-105.
9. Hobaus C, Herz C, Schernthaner GH. Do we need a new classification system for arteriosclerotic lesions in crural

https://doi.org/10.22467/jwmr.2020.01277

limb ischemia? Pros and cons. Atherosclerosis 2016;251:493-4.
10. Gey DC, Lesho EP, Manngold J. Management of peripheral arterial disease. Am Fam Physician 2004;69:525-32.
11. Miller JM, Dewey M, Vavere AL, et al. Coronary CT angiography using 64 detector rows: methods and design of the multi-centre trial CORE-64. Eur Radiol 2009;19:816-28.
12. Bollinger A, Breddin K, Hess H, et al. Semiquantitative assessment of lower limb atherosclerosis from routine angiographic images. Atherosclerosis 1981;38:339-46.
13. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013;36 Suppl 1(Suppl 1):S67-74.
14. American Diabetes Association. Peripheral arterial disease in people with diabetes. Diabetes Care 2003;26:3333-41.
15. Brechow A, Slesaczeck T, Munch D, et al. Improving major amputation rates in the multicomplex diabetic foot patient: focus on the severity of peripheral arterial disease. Ther Adv Endocrinol Metab 2013;4:83-94.
16. Mills JL Sr, Conte MS, Armstrong DG, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on Wound, Ischemia, and foot Infection (WIfI). J Vasc Surg 2014;59:220-34.
17. van der Feen C, Neijens FS, Kanters SD, et al. Angiographic distribution of lower extremity atherosclerosis in patients with and without diabetes. Diabet Med 2002;19:366-70.
18. Graziani L, Silvestro A, Bertone V, et al. Vascular involvement in diabetic subjects with ischemic foot ulcer: a new morphologic categorization of disease severity. Eur J Vasc Endovasc Surg 2007;33:453-60.
19. Hadavand F, Amouzegar A, Amid H. Pro-calcitonin, erythrocyte sedimentation rate and C-reactive protein in predicting diabetic foot ulcer characteristics; a cross sectional study. Arch Acad Emerg Med 2019;7:37.
20. Jonaidi Jafari N, Safaie-Firoozabadi M, Safaie-Firoozabadi MS, et al. Comparison of ESR, CRP and WBC count as inflammatory marker in patients with infected and non-infected diabetic foot. J Babol Univ Med Sci 2012;14:71-7.
21. Zhang SS, Tang ZY, Fang P, et al. Nutritional status deteriorates as the severity of diabetic foot ulcers increases and independently associates with prognosis. Exp Ther Med 2013;5:215-22.
22. Hobizal KB, Wukich DK. Diabetic foot infections: current concept review. Diabet Foot Ankle 2012;3:18409.
23. Xia N, Morteza A, Yang F, et al. Review of the role of cigarette smoking in diabetic foot. J Diabetes Investig 2019;10:202-15.